97. The method according to claim 77, wherein the morphogenic protein comprises OP-1 at a concentration of from about 1 ng/ml to about 500 ng/ml and the morphogenic protein stimulatory factor comprises insulin at a concentration of from about 0.01 nM to about 1000 nM.

98. The method according to claim 77, wherein the morphogenic protein comprises OP-1 at a concentration of from about 1 ng/ml to about 500 ng/ml and the morphogenic protein stimulatory factor comprises parathyroid hormone at a concentration of from about 10 nM to about 1000 nM.

99. The method according to claim 98, wherein OP-1 is about 200 ng/ml and parathyroid hormone is about 25-200 nM.

100. The method according to claim 77, wherein the morphogenic protein comprises OP-1 at a concentration of from about 1 ng/ml to about 500 ng/ml and the morphogenic protein stimulatory factor comprises progesterone at a concentration of from about 0.05 nM to about 1000 nM.

101. The method according to claim 100, wherein OP-1 is about 200 ng/ml and progesterone is about 0.05 - 5 nM. --.

REMARKS

This is a division of pending application 09/158,220, filed September 22, 1998 ("the '220 parent application"), which is a division of United States application 09/027,873, filed February 23, 1998 and which issued as United States patent 5,854,207, which is a division of United States application 08/570,752, filed December 12, 1995. Aplicants have filed this divisional application to

prosecute separately and obtain allowance of subject matter that was canceled from the '220 parent application as a result of a restriction requirement (Paper Number 4, mailed November 2, 1998).

Applicants have amended the specification to add at the beginning of the application a section entitled "TECHNICAL FIELD OF THE INVENTION". Support for this amendment is found in the application as originally filed in the ABSTRACT (p. 109).

Applicants have also amended the specification by referring to and incorporating by reference the parent applications, from which the instant application claims priority, in a section entitled "CROSS REFERENCE TO RELATED APPLICATIONS".

Applicants have canceled claims 1-68 and added claims 78-104. As a result, claims 69-104 are pending in this application.

Claims 69, 74, and 76 have been amended to remove dependency on their base claims (claim 30 or 60), which have been allowed in the '220 parent application and thus canceled in this application. Applicants have also amended claim 77 and added claims 78-104 to remove references to canceled claims 1-29. Support for added claims 78-104 can be found in original claims 1-29. Claim 71 is amended to correct a typographical error.

No new matter has been introduced by any of the above amendments.

New claims 78-101 are essentially the same as claims 93-119 presented in the September 22, 1998 Preliminary Amendment of the '220 parent application. The only substantive difference is that claims 78-104 of this application do not recite multiple dependencies.

During prosecution of the '220 parent application, claims 69-77 and 93-119 were divided into four groups of inventions. During a telephonic interview between the Examiner and applicants' counsel on October 29, 1998, the Examiner indicated that he would consider all of those claims in a single divisional application if the claims were amended to remove multiple dependencies and to define a "morphogenic protein" as "being capable of inducing tissue formation when accessible to a progenitor cell." The claim amendments set forth above are consistent with the Examiner's suggestions.

INFORMATION DISCLOSURE STATEMENT

Pursuant to 37 C.F.R. §§ 1.56 and 1.97, applicants make of record the following documents*:

United States Patents

Oppermann, et al.	5,011,691	April 30, 1991
Kuberasampath, et al.	5,108,753	April 28, 1992
Kuberasampath, et al.	5,162,114	November 10, 1992
Kuberasampath, et al.	5,171,574	December 15, 1992
Oppermann, et al.	5,258,494	November 2, 1993
Oppermann, et al.	5,324,819	June 28, 1994
Rueger, et al.	5,344,654	September 6, 1994
Oppermann, et al.	5,354,557	October 11, 1994
Wozney, et al.	5,459,047	October 17, 1995
Rodan, et al.	5,461,034	October 24, 1995

* Each of the cited documents was enclosed with applicant's June 1, 1998 Information Disclosure Statement in the 09/027,873 application from which the present application claims priority under 35 U.S.C. § 120. If the Examiner desires, applicant will provide copies of these documents.

Foreign Patents or Published Applications

Genetics Institute, Inc.	WO 95/05846	published March 2, 1995
Genetics Institute, Inc.	WO 95/16034	published June 15, 1995
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Andrews, P. W. et al., "Inhibition of Proliferation and Induction of Differentiation of Pluripotent Human Embryonal Carcinoma Cells by Osteogenic Protein-1 (Or Bone Morphogenetic Protein-7)," Laboratory Investigation 71:243-251 (1994).

Benayahu, D., et al., "Differential Effects of Retinoic Acid and Growth Factors on Osteoblastic Markers and CD10/NEP Activity in Stromal-Derived Osteoblasts," Journal of Cellular Biochemistry 56:62-72 (1994).

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Cook, Stephen D., et al., "Recombinant Human Bone Morphogenetic Protein-7 Induces Healing in a Canine Long-Bone Segmental Defect Model," Clinical Orthopaedics & Related Research 201:302-312 (April 1994).

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Cook, Stephen D., et al., "Effect of Recombinant Human Osteogenic Protein-1 on Healing of Segmental Defects in Non-Human Primates," The Journal of Bone and Joint Surgery 77-A:734-750 (May 1995).

Dudley, A.T. et al., "A Requirement for Bone Morphogenetic Protein-7 During Development of the Mammalian Kidney and Eye," Genes and Development 9:2795-2807 (November 1995).

Gabbitas, Bari, et al., "Bone Morphogenetic Protein-2 Inhibits the Synthesis of Insulin-Like Growth Factor-Binding Protein-5 in Bone Cell Cultures," The Endocrine Society 136:2397-2403 (1995).

Gitelman, Stephen E., et al., "Recombinant Vgr-1/BMP-6-expressing Tumors Induce Fibrosis and Endochondral Bone Formation In Vivo," J. Cell Biol. 126:1595-1609 (1994).

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Hammerman, Marc R., "Growth Factors in Renal Development," Seminars in Nephrology 15:291-299 (July 1995).

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Hentunen, T.A. et al., "Effects of Recombinant Human Osteogenic Protein-1 on the Differentiation of Osteoclast-like Cells and Bone Resorption," Biochemical and Biophysical Research Communications 209:433-443 (April 17, 1995).

Hiraki, Yuji, et al., "Bone Morphogenetic Proteins (BMP-2 and BMP-3) Promote Growth and Expression of the Differentiated Phenotype of Rabbit Chondrocytes and Osteoblastic MC3T3-E1 Cells In Vitro," Journal of Bone and Mineral Research 6:1373-1385 (December 1991).

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Knutsen, R., et al., "Osteogenic Protein-1 Stimulates Proliferation and Differentiation of Human Bone Cells in Vitro," Biochemical and Biophysical Research Communications 194:1352-1358 (August 16, 1993).

Knutsen, R., et al., "Regulation of Insulin-Like Growth Factor System Components by Osteogenic Protein-1 in Human Bone Cells," Endocrinology 136:857-865 (March 1995).

Liem, Karel, Jr., et al., "Dorsal Differentiation of Neural Plate Cells Induced by BMP-Mediated Signals from Epidermal Ectoderm," Cell 82:969-979 (September 22, 1995).

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Ripamonti, U. and S. Vukicevic, "Bone Morphogenetic Proteins: From Developmental Biology to Molecular Therapeutics," So. Afr. J. Sci. 91:277-80 (June 1995).

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Sampath, T. K. and A.H. Reddi, "Dissociative extraction and reconstitution of extracellular matrix components involved in local bone differentiation," Proc. Natl. Acad. Sci. - Cell Biology 78:7599-7603 (December 1981).

Sampath, T. Kuber, et al., "Recombinant Human Osteogenic Protein-1 (hOP-1) Induces New Bone Formation *in Vivo* with a Specific Activity Comparable with Natural Bovine Osteogenic Protein and Stimulates Osteoblast Proliferation and Differentiation *in Vitro*," J. Biol. Chem. 267:20352-20362 (October 5, 1992).

Sampath, T. Kuber, et al., "Role Of Osteogenic Protein-1 (OP-1) In Growth, Development And Repair Of Bone," J. Cellular Biochem. Supplemental 17E:147 (1993).

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Vukicevic, S., et al., "Discovery and Clinical Applications of Bone Morphogenetic Proteins," Eur. J. Clin. Chem. Clin. Biochem. 33:661-671 (October 1995).

Wozney, John M., "The Potential Role of Bone Morphogenetic Proteins in Periodontal Reconstruction," J. Periodontol. 66:506-510 (1995).

In addition, Applicants make of record the following documents in the above-identified application, which were cited in a European Search Report in connection with Applicants' counterpart International patent application:

Foreign Patents or Published Applications

WO 93/05823-A (Baylink D. et al.)	published April 1, 1993
WO 92/21365-A (Proctor & Gamble)	published December 10, 1992
WO 92/09697-A (Celtrix Laboratories)	published June 11, 1992
EP 0 514 720-A (Celtrix Pharmaceuticals)	published November 25, 1992
EP 0 436 469-A (Ciba Geigy)	published July 10, 1991
JP 9048738-A (Snow Brand Milk Prod.)	published February 18, 1997

Applicants request that these publications be (1) fully considered by the Patent and Trademark Office during the

examination of this application; and (2) printed on any patent which may issue on this application.

Applicants request that a copy of Form PTO-1449, as considered and initialed by the Examiner, be returned with the next communication.

This Statement is submitted less than three months from the application filing date and before the mailing date of the first substantive Office Action. In accordance with 37 C.F.R. § 1.97, submission of this Statement requires no fee.

The Commissioner, however, is hereby authorized to charge payment of any additional fees required in connection with this Information Disclosure Statement to Deposit Account No. 06-1075. A duplicate copy of this letter is transmitted herewith.

CONCLUSION

In view of the foregoing remarks, applicants respectfully request consideration and allowance of pending claims 69-101.

Respectfully submitted

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